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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/043,933	03/30/1998	JEAN-MARC BALLOUL	017753-094	7553

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	**PAPER NUMBER**
1648	31

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/043,933	BALLOUL ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-20,25-31,79,80,82,83,85-92,94,95 and 97-120* is/are pending in the application.

4a) Of the above claim(s) *10-20,25-31,86,100 and 112* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *79,80,82,83,85,87-92,94,95,97-99,101-111 and 113-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

In paper no. 30, Applicant cancelled claims 81, 84, 93, 96 and amended claims 79, 80, 82, 83, 85, 88, 89, 91, 92, 94, 95, 97, 104, 105, 107-109 and 116-120. Claims 10-20, 25-31, 79, 80, 82, 83, 85-92, 94, 95 and 97-120 are pending. Claims 10-20 and 25-31 are withdrawn from consideration due to a non-election of invention in paper no. 8. Claims 86, 100 and 112 are also withdrawn from consideration directed to an invention that is independent or distinct from the invention originally claimed. Applicant is reminded to cancel the claims 10-20, 25-31, 86, 100 and 112 drawn to the non-elected invention. Claims 79, 80, 82, 83, 85, 87-92, 94, 95, 97-99, 101-111, 113-120 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 79, 80, 82, 83, 85, 87-92, 94, 95, 97-99, 101-111, 113-120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant has amended independent claims 79, 91 and 108 to recite "consisting essentially of", rather than "comprising".

Applicant's amendments to the claims have been carefully reviewed, but do not overcome the rejection because it is not evident which elements are intended to be excluded from the claimed compositions. The MPEP § 2111.03 states that "absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising"." Therefore, the amended

transitional phrase is interpreted as open claim language and the rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 79, 82, and 87-90 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Stanley et al. (US 6,096,869) for reasons of record.

Applicant initially notes the amendment to the transitional phrase in the claims. Applicant also submits that Stanley et al. do not consider administering the papillomavirus polypeptides in the absence of IL-12.

Applicant's arguments, as well as a careful review of the reference, have been considered, but are found unpersuasive. As discussed above, it cannot be determined which ingredients are encompassed within the compositions. More specifically, it cannot be discerned which ingredients would materially affect the instant compositions and are intended to be

excluded by the transitional phrase "consisting essentially of". Therefore, since the transitional phrase in the claim encompasses open claim language, the additional component of IL-12 anticipates the instantly claimed formulations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 91, 98, 99, 101-108, 110, and 115-120 rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al. supra, Galloway. (Infectious Agents and Disease. 1994; 3: 187-193), Hines et al. Obstetrics and Gynecology. 1995; 86 (5): 860-866), and Gajewski. The Journal of Immunology. 1996; 156: 465-472) for reasons of record.

Applicant lists the three criteria that must be met to establish a prima facie case of obviousness and discusses the differences in expression between IL-12 and IL-2 in the working examples of Stanley et al. Applicant asserts that Stanley et al. teach away from the instant composition because the reference only administers IL-12, does not suggest administering another cytokine, and does not suggest a reasonable expectation of success in treating papillomavirus with any other cytokine. Applicant concludes that the ordinary artisan would not be motivated to administer another cytokine in view of the teachings of Stanley et al.

Applicant's arguments, as well as a careful review of the reference, have been fully considered, but are found unpersuasive. It is maintained that the teachings of Stanley et al. clearly indicate the importance of administering a cytokine with a papillomavirus pharmaceutical

composition. This is evident in the claims as well as the data provided in the working examples of Stanley et al. Stanley et al. provide a profile of cytokines present in various papillomavirus-infected tissue and provides a detailed analysis in several tables. (Although these tables are discussed in the patent, they are not illustrated. The Examiner was able to find a copy of the data and tables discussed by Applicant in Stanley et al. WO 96/29091. It is evident that Applicant also has access to the data in the tables of Stanley et al. since an exact number of samples containing various cytokines is discussed in Applicant's response.) The data presented by Stanley et al. establishes that cytokines are present papillomavirus tissue pathologies and are a central aspect of papillomavirus infection. Stanley et al. also emphasize the importance of administering a cytokine with a papillomavirus polypeptide, see the claims and the working examples.

Although Stanley et al. do not teach administering IL-2, it is evident from the teachings of Hines et al. that one of ordinary skill would have been motivated to administer IL-2 to treat papillomavirus infections. Hines et al. treat papillomavirus infections by administering lymphocytes that are stimulated with various papillomavirus polypeptides and IL-2. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to treat papillomavirus infections by administering papillomavirus polypeptides with IL-2 to stimulate T cells *in vivo*. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the instant invention because both Hines et al. and Stanley et al. use cytokines and various papillomavirus polypeptides to treat papillomavirus infections. Therefore, it is evident from the teachings of Stanley et al. and Hines et al. that using cytokines in conjunction with papillomavirus polypeptides is a conventional

treatment strategy for ameliorating and preventing papillomavirus infection in the art. Applicant has not demonstrated an unexpected result with the claimed combination. Therefore, it is maintained that it would have been prima facie obvious to the ordinary artisan to administer a cytokine and at least one papillomavirus polypeptide to reduce papillomavirus pathologies.

Applicant argues that the instant invention differs from the teachings of Hines et al. because the invention administers IL-2 directly. Applicant also asserts that prior to the invention, it was not known whether cytokines and HPV polypeptides would adequately stimulate a host's cells against infection.

Applicant's arguments have been carefully considered, but are found unpersuasive because direct administration of a cytokine with papillomavirus polypeptides is taught by Stanley et al. Also, it is clear from the teachings of Stanley et al. and Hines et al. that combining a cytokine with papillomavirus polypeptides is an effective treatment to eliminate papillomavirus infections.

Applicant also argues that Galloway does not suggest administering a cytokine with HPV polypeptides.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Galloway is not required to teach a limitation already established by the teachings of Stanley et al. and Hines et al. Galloway discusses the prophylactic properties of L1 and L2 and the ameliorative

properties of E6 and E7. This discussion provides a strong motivation to combine early and late polypeptides into a papillomavirus vaccine to prevent or treat infection.

Applicant asserts that Gajewski does not demonstrate that any B7.1-transfected autologous tumor cells would adequately stimulate CD8 production.

Applicant's arguments and a careful review of the reference have been considered, but are found unpersuasive. The focus of Gajewski is that B7.1 costimulates CD8+ T cells to induce the production of IL-2. Also, Gajewski summarizes teachings in the prior art directed to the broad applicability and long-term protection of expressing B7.1 on human tumor cells, see the discussion section. Since papillomavirus is directly linked to the formation of human tumor cells, administration of the B7.1 molecule of Gajewski would also stimulate the production of IL-2.

Applicant also argues that Gajewski does not suggest combining HPV polypeptides with the B7.1 molecule or provide any expectation of success for inducing a therapeutic effect by co-administration.

In response, Gajewski is not required to specifically teach administering HPV polypeptides with B7.1. If the reference taught these elements together, the reference would have been considered under 35 USC § 102. As Applicant pointed out at the beginning of the response, one of the elements required to establish a prima facie case of obviousness is for the combination of references to teach every limitation claimed. Stanley et al., Galloway and Hines et al. do not teach B7.1, but this element is taught by Gajewski. Stanley et al. and Hines et al. teach specific utilization of a cytokine and papillomavirus polypeptides to treat infection. Gajewski teaches another cytokine that is useful for ameliorating human tumors. Although

Gajewski does not teach specific administration of this cytokine, Stanley et al. directly administers a cytokine to treat papillomavirus infection, which demonstrates a more than reasonable expectation of success for administering a cytokine to induce a therapeutic effect against tumor formation.

In conclusion, a prima facie obviousness case has been established. All of the references teach all of the instant limitations. The combined references also provide at least one motivation for modifying specific elements and provide one of ordinary skill in the art a more than reasonable degree of expectation for producing the claimed invention.

Claims 80, 81, 83-85, 92-97, 109, 113, and 114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanley et al., Galloway, Hines et al., and Gajewski as applied to claims 79, 82, 87-91, 91, 98, 99, 101-108, 110, and 115 above, and further in view of Crook et al. (Cell. 1991; 67: 547-556) and Munger et al. (EMBO Journal. 1989; 8: 4099-4105) for reasons of record.

Applicant asserts that Crook et al. and Munger et al. are used only to provide motivation to use specific E6 and E7 variants in the composition, but do not remedy difficiencies asserted by Applicant.

Applicant's assertion has been considered, but is not persuasive in refuting the combined teachings of Stanley et al., Galloway, Hines et al., and Gajewski.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
January 23, 2003

JAMES HOUSEL 1/27/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600